AMENDMENTS TO THE SPECIFICATION

Please replace paragraph [006] with the following amended paragraph:

[006] In accordance with the present invention, a method of treatment or prevention of damage due to radiation exposure comprising administering to a subject in need of such treatment an effective amount of a composition comprising 1) a compound including a radiation damage-inhibiting polypeptide comprising amino acid sequence LKKTET [SEQ ID NO: 1], a conservative variant of LKKTET [SEQ ID NO: 1], an actin-sequestering agent, an anti-inflammatory agent; 2) an agent which stimulates production of said compound in said subject; 3) an agent which regulates said compound in said subject; or 4) an antagonist of said compound, so as to inhibit radiation damage in said subject.

Please replace paragraph [007] with the following amended paragraph:

[007] In accordance with one embodiment, the present invention relates generally to the treatment, prevention or reversal of physical, cognitive, and biological injuries resulting from exposure to ionizing radiation by the use of the peptide, Thymosin beta 4 (Thymosin β4 or Tβ4), or fragments of Tβ4 such as LKKTET [SEQ ID NO: 1], or conservative variants thereof. Sometimes these are referred to as LKKTET [SEQ ID NO: 1] peptides or polypeptides. Included are N- or C-terminal variants such as KLKKTET [SEQ ID NO: 2] and LKKTETQ [SEQ ID NO: 3].

Please replace paragraph [009] with the following amended paragraph:

[009] Without being bound to any particular theory, it is believed that the present invention is based on the discovery that anti-inflammatory peptides and actin-sequestering peptides such as Tβ4 and a number of other actin-sequestering peptides which contain the actin binding motif and amino acid sequence LKKTET [SEQ ID NO: 1], are useful for the

treatment or prevention of certain biological processes which occur due to exposure to ionizing radiation, and promote treatment or prevention of damage due to ionizing radiation exposure. These peptides have the capacity to promote repair and healing by having the ability to induce terminal deoxynucleotidyl transferase (a non-template directed DNA polymerase), to decrease the levels of one or more inflammatory cytokines and chemokines and to act as a chemotactic and angiogenic factors for endothelial cells, and thus prevent and/or heal and reverse effects that occur due to a number of factors, including exposure to certain x-rays, gamma-rays or other forms of ionizing radiation and radiotherapy of (i) cancer patients, (ii) patients receiving radiation or photo-therapy for skin disorders, or (iii) individuals exposed to acute or lethal doses of ionizing radiation. Tβ4 may act as a "rescue molecule", preventing permanent polymerization of actin, preserving the function of actin in cells exposed to radiation and protecting the ability of normal cells to divide. Tβ4 may inhibit induction of enzymes which induce apoptosis, thereby inhibiting induction of apoptosis of normal cells which may be caused by radiation. Tβ4 may also prevent damage to tissue by modulation of transcription factors associated with improved survival of tissue. Tβ4 forms a functional ternary complex with LIM domain protein PINCH and Integrin Linked Kinase (ILK), which are essential for cell survival. Tβ4 exposure results in induction, altered localization and activation of ILK. Formation of a Tβ4-PINCH-ILK complex in cells may mediate the protection and/or repair effects of Tβ4 independently of actin polymerization. Additionally, Tβ4 stimulates the production of laminin-5 in cells which may protect, or facilitate repair of, tissue.

Please replace paragraph [0011] with the following amended paragraph:

[0011] In accordance with one embodiment, the invention is a method of treatment or prevention of damage due to ionizing radiation exposure comprising administering to a subject in need of such treatment an effective amount of a composition comprising a radiation damage-inhibiting polypeptide comprising LKKTET[SEQ ID NO: 1], or a conservative variant thereof having radiation damage-inhibiting activity, preferably Tβ4, an

isoform of Tβ4, oxidized Tβ4, Tβ4 sulfoxide, or an antagonist of Tβ4. Administration can be before, during or after exposure of the subject to radiation, so as to protect tissue and prevent damage, and/or salvage and repair tissue.

Please replace paragraph [0012] with the following amended paragraph:

[0012] Preferred compositions which may be used in accordance with the present invention comprise amino acid sequence LKKTET [SEQ ID NO: 1], amino acid sequence KLKKTET [SEQ ID NO: 2] or LKKTETQ [SEQ ID NO: 3], Tβ4, an N-terminal variant of Tβ4, a C-terminal variant of Tβ4, an isoform of Tβ4, a splice-variant of Tβ4, oxidized Tβ4, Tβ4 sulfoxide, lymphoid Tβ4, pegylated Tβ4 or any other actin sequestering or bundling proteins having actin binding domains, or peptide fragments comprising or consisting essentially of the amino acid sequence LKKTET [SEQ ID NO: 1] or conservative variants thereof, having radiation damage-inhibiting activity. International Application Serial No. PCT/US99/17282, incorporated herein by reference, discloses isoforms of Tβ4 which may be useful in accordance with the present invention as well as amino acid sequence LKKTET [SEQ ID NO: 1] and conservative variants thereof, which may be utilized with the present invention. International Application Serial No. PCT/GB99/00833 (WO 99/49883), incorporated herein by reference, discloses oxidized Tβ4 which may be utilized in accordance with the present invention. Although the present invention is described primarily hereinafter with respect to Tβ4 and Tβ4 isoforms, it is to be understood that the following description is intended to be equally applicable to amino acid sequence LKKTET [SEQ ID NO: 1], KLKKTET [SEQ ID NO: 2], LKKTETQ [SEQ ID NO: 3], peptides and fragments comprising or consisting essentially of LKKTET [SEQ ID NO: 1], KLKKTET [SEQ ID NO: 2] or LKKTETQ [SEQ ID NO: 3], conservative variants thereof, as well as oxidized Tβ4 and Tβ4 sulfoxide, having radiation damage-inhibiting activity.

Please replace paragraph [0016] with the following amended paragraph:

[0016] Tβ4 isoforms have been identified and have about 70%, or about 75%, or about 80% or more homology to the known amino acid sequence of Tβ4. Such isoforms include, for example, $T\beta4^{ala}$, Tβ9, Tβ10, Tβ11, Tβ12, Tβ13, Tβ14 and Tβ15. Similar to Tβ4, the Tβ10 and Tβ15 isoforms have been shown to sequester actin. Tβ4, Tβ10 and Tβ15, as well as these other isoforms share an amino acid sequence, LKKTET [SEQ ID NO: 1], that appears to be involved in mediating actin sequestration or binding. Although not wishing to be bound to any particular theory, the activity of Tβ4 isoforms may be due, in part, to the ability to regulate the polymerization of actin. For example, Tβ4 can modulate actin polymerization in skin (e.g. β-thymosins appear to depolymerize F-actin by sequestering free G-actin). Tβ4's ability to modulate actin polymerization may therefore be due to all, or in part, its ability to bind to or sequester actin via the LKKTET [SEQ ID NO: 1], sequence. Thus, as with Tβ4, other proteins which bind or sequester actin, or modulate actin polymerization, including Tβ4 isoforms having the amino acid sequence LKKTET [SEQ ID NO: 1], are likely to prevent or reduce radiation damage alone or in a combination with Tβ4, as set forth herein.

Please replace paragraph [0018] with the following amended paragraph:

[0018] In addition, other proteins having actin sequestering or binding capability, or that can mobilize actin or modulate actin polymerization, as demonstrated in an appropriate sequestering, binding, mobilization or polymerization assay, or identified by the presence of an amino acid sequence that mediates actin binding, such as LKKTET [SEQ ID NO: 1], for example, can similarly be employed in the methods of the invention. Such proteins include gelsolin, vitamin D binding protein (DBP), profilin, cofilin, adsevertin, propomyosin, fincilin, depactin, DnaseI, vilin, fragmin, severin, capping protein, β-actinin and acumentin, for example. As such methods include those practiced in a subject, the invention further provides pharmaceutical compositions comprising gelsolin, vitamin D binding protein (DBP), profilin, cofilin, depactin, DnaseI, vilin, fragmin, severin, capping

protein, β-actinin and acumentin as set forth herein. Thus, the invention includes the use of a radiation damage-inhibiting polypeptide comprising the amino acid sequence LKKTET [SEQ ID NO: 1] (which may be within its primary amino acid sequence) and conservative variants thereof.

Please replace paragraph [0026] with the following amended paragraph:

[0026] In one embodiment, the invention provides a method for treatment or prevention of damage due to ionizing radiation exposure comprising administering to a subject in need of such treatment, an effective amount of a composition comprising a radiation damage-inhibiting polypeptide comprising amino acid sequence LKKTET [SEQ ID NO: 1], or a conservative variant thereof having radiation damage-inhibiting activity.

Please replace paragraph [0028] with the following amended paragraph:

[0028] The invention provides a method for the prevention and/or healing and reversal of the body, bodily tissues, and organs and/or symptoms associated therewith, resulting from X-rays, gamma-rays or other forms of ionizing radiation and radiotherapy of (i) cancer patients, (ii) patients receiving radiation or photo-therapy for skin or other disorders, or (iii) individuals exposed to acute or lethal doses of ionizing radiation, by the application of a therapeutically effective amount of a composition comprising Tβ4, Tβ4 analogues, isoforms, or peptide fragments with the amino acid sequence LKKTET [SEQ ID NO: 1] and conservative variants thereof.

Please replace paragraph [0031] with the following amended paragraph:

[0031] A method of the invention involves utilization of a composition which contains an agent that stimulates the production of LKKTET [SEQ ID NO: 1] or Tβ4 or variants thereof or some other actin-sequestering or anti-inflammatory compound.

Please replace paragraph [0035] with the following amended paragraph:

[0035] One method includes treating exposure to ionizing radiation or other types of radiation in a subject, comprising administering to the subject a composition containing an agent that regulates the actin-sequestering peptide, LKKTET [SEQ ID NO: 1], or Tβ4 activity. The agent may be an antibody. The antibody may be polyclonal or monoclonal.

Please replace paragraph [0038] with the following amended paragraph:

[0038] The invention may permit significantly increasing the amount of radiotherapy that a cancer patient can receive by administering an effective dose of Tβ4, or Tβ4 analogues, isoforms, or other molecules described herein, containing the amino acid sequence LKKTET [SEQ ID NO: 1] and other conservative variants that reduce inflammation, and/or actin toxicity, and/or stimulate angiogenesis and protect radio-sensitive stem cells in the blood, bone marrow, gastrointestinal tract and/or other parts of the body.